Human Pluripotent Stem Cells to Assess Developmental Toxicity in the Osteogenic Lineage.

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Public Summary:
Musculoskeletal birth defects are frequent, yet their causes remain insufficiently investigated. Aside from genetic factors, exposure to environmental toxicants is suspected to contribute to the etiology of skeletal malformations. However, most chemicals in the environment are insufficiently characterized for their potential to cause harm to the differentiation of osteoblasts, the bone-forming cells and thereby the development of the skeleton.This lack of information primarily stems from animal testing being prohibitively expensive and time-consuming, which has prompted the development of predictive in vitro alternative methods. With the advent of mouse embryonic stem cells, which represent cells with the potential to become any of the 200 cell types in the body, among them osteoblasts, the past 15 years have borne suitable opportunities to assess chemicals in vitro. However, with an increasing understanding of the differences between mouse and human embryonic development, a need for human-specific developmental toxicity testing has risen. This chapter provides a detailed protocol on how to differentiate human embryonic stem cells into the osteogenic lineage, how to assess differentiation inhibition and how to evaluate such findings in relation to the mitochondrial activity of human embryonic stem cells and human fibroblasts, while exposed to a potential toxicant. Together, these endpoints allow for a human-specific screening of developmental toxicity specifically related to the osteogenic lineage

Scientific Abstract:
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